IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Giancotti Application No.: 10/595,845 Filed: 05/16/2006 Title: Method for controlling pathological angiogenesis by inhibition of a6b4 integrin Attorney Docket No.: MSK.P-076 Customer No.: 52334	Group Art Unit: 1644 Examiner: M.M. Haddad Confirmation No: 7804

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

RESPONSE TO OFFICE ACTION

This is in response to the Office Action mailed May 13, 2009 for the above-captioned application. Reconsideration and further examination are respectfully requested.

An extension of time sufficient to make this paper timely is requested and the fee is enclosed. The fee is paid as a large entity and the prior claim to small entity status is hereby withdrawn.

Mischaracterization of Invention

Paragraph 4 of the office action provides a summary of the claimed invention. Applicants point out that this summary is incomplete, since it does not include the inhibition of signaling function which is recited in the claims.

Double Patenting Rejection

The Examiner has provisionally rejected claims 1-3, 5, 7-9, 15, 17, 19 and 21-22 for obviousness-type double patenting over copending application 10/596,364. Applicants point out that the claims of this application are directed to inhibition of angiogenesis, not inhibition of initiation of primary or metastatic tumor growth as in the cited application. The Examiner has

not addressed the differences in the claims in making this rejection, and indeed erroneously states that the claims are all directed to inhibition of tumorigenesis. Furthermore, Applicants challenge the authority of the US Patent and Trademark Office, and administrative agency, to apply a rule developed in equity by the Courts. Nothing in the treatment of this rule by the Patent and Trademark Office considers equitable principles, nor is an administrative agency empowered to act in equity outside of the guidelines of properly promulgated regulations. There are no laws or regulations relating to the standards for obviousness-type double patenting and therefore in making this rejection the Patent Examiner and the Patent and Trademark Office are exceeding their authority. Thus, this rejection is believed to be both improper and in error and withdrawal is requested.

Inherent Inconsistency in the Examiner's Position

In rejecting the claims of this application under both § 112, first paragraph and § 103, the Examiner has argued that the Examples in the specification are presumed not to have the stated characteristics, whilst compositions are the cited art are presumed to have these characteristics. There is no technical argument made to justify this differential treatment of antibodies. Applicants respectfully invite the Examiner to choose one position, and to support it with substantiated reasoning and to drop the rejection that is inconsistent with what the examiner chooses to perceive as based on supportable assertions.

Written Description

Claims 1-3, 5, 7-9, 15, 17 and 19 stand rejected under 35 USC § 112, first paragraph, as lacking written description. It is noted that this rejection also contains a statement (¶ 9, sub-¶ 2) that seems to be directed to enablement rather than written description. There is therefore a lack of clarity as to just what the basis for the rejection is. If both rejections are intended, then consistent with teir being separate rejections they should be presented separately.

This rejection now focuses on the agent that targets β4, and the Examiner states that the specification does not contain a representative number of species, nor does it provide a description of structural features that are common to the species. This focus on the number of examples, or the asserted requirement for actual structures in all cases is inconsistent with applicable law. Thus, MPEP § 2163 states

> Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. As explained by the Federal Circuit, "(1) examples are not necessary to support the adequacy of a

> written description; (2) the written description standard may be met even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006).

Thus, the standards set forth by the Examiner are permissive ways in which written description **may** be satisfied, but they are not mandatory. The examiner has offered no clear statement apart from "not enough examples" as to why a person skilled in the art would not recognize the inventors as having possession of the claimed invention. See also Example 12 in the Training Materials at http://www.uspto.gov/web/menu/written.pdf

In response to Applicants' previous arguments, the Examiner states (Page 4) that "it is the Examiner's position that the prior [sic, art?] of Sepp et al teachings (sic, teaches?) that inhibiting the signaling function of β4 does not lead to the inhibition of angiogenesis." The examiner has not explained what it is about the Sepp article that he believs justifies this conclusion. The examiner has also not responded to Appilcants discussion of the reference:

> Sepp merely discloses that use of two specific promoters of angiogenesis (bFGF and PMA) lead to a reduction of β4. The Examiner's argument ignores cause and effect, as well as the many reasons β4 may be reduced. The Examiner also ignores the statement that bFGF stimulation of bovine adrenal cortex endothelial cells induces an <u>increase</u> in β4 production. Sepp, at 270. In addition, as the Examiner has pointed out, the two functions of β4- adhesion and signaling- are quite separate. It is entirely plausible both that reduction of β4 adhesion would lead to angiogenesis and reduction of β4 signaling would lead to antiangiogenesis. Sepp does not provide any information about which <u>function</u> of β4 is reduced; it merely states that overall β4 is reduced. The experimental data provided in the specification shows that inhibition of signaling does have an antiangiogenic effect. The present invention concerns a reduction in the amount of signaling function of B4, not overall β4.

For these reasons, Applicants submit that the written description rejeciotn is in error and must be withdrawn.

<u>Anticipation - Land</u>

In addition, the Examiner has maintained his rejection under 35 USC § 102(b)/(e) for anticipation by Land (US Pat. Pub. 20030224993). To support the rejection in the absence of any teaching concerning angiogenesis in the reference, the Examiner argues on Page 6 of the office

action that "all of the cancer condition [sic] taught by the prior art of Land are prone to pathological angiogenesis." This argument fails to take into account that angiogenesis is something that occurs after a period of tumor growth, so that cells of a given cancer type may not be secreting agents to stimulate angiogenesis. In addition, the tissue in which a tumor is located may not be prone to angiogenesis even if the tumor is secreting such agents. There are no experiments described in Land (even prophetically) that would assess effect on angiogenesis. Thus, there is no basis to assume that anything concerning angiogenesis occurred inherently in Land.

It is further pointed out that the Examiner is unfairly making unchallengeable allegations about the presumed qualities of the Land antibodies, since no specific antibodies are disclosed in Land in a manner which would permit comparative testing. Indeed, there is no indication in Land that any antibody was ever made.

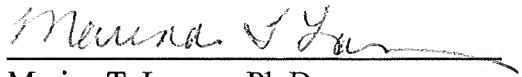
Finally, Applicants note that the Examiner seems to confusing the standards for patentability of compositions, which do not become patentable simply because a mechanisms of action is discovered, and patentability of method claims. The present claims are method claims, and the mechanism, scope and nature of the activity is highly relevant to how a composition is used, making method claims patentable even for old compositions.

As Land does not disclose all of the elements of the current claimed invention expressly or inherently, it does not anticipate, and this rejection is in error.

Anticipation - Abdel-Ghany

The Examiner has also cited a new reference, Abdel-Ghany et al. as anticipating claims 1-3, 5, 7-9, 15, 17, 19, 21 and 22. Abdel-Ghany, like Land, is silent with respect to angiogenesis, and indeed focuses on adhesion (i.e., binding) of cancer cells by binding a newly identified ligand, hCLCA2, to β4. There is no discussion of signaling function, and the only use of antibodies is to confirm binding affinity. Thus, Abdel-Ghany is deficient and not anticipatory for the same reasons as Land.

Respectfully submitted,



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